

United States Patent
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AT₄ receptor ligands as angiogenic, anti-angiogenic, and anti-tumor agents

Abstract

AT₄ receptor agonists are potent activators of angiogenesis and can be used to treat diseases that are characterized by vascular insufficiency. AT₄ receptor antagonists, which are potent inhibitors of angiogenesis, and can be used as anti-angiogenic agents for the treatment of cancer, diabetic retinopathy, rheumatoid arthritis, psoriasis, atherosclerotic plaque formation, and any disease process that is characterized by excessive, undesired or inappropriate angiogenesis or proliferation of endothelial cells.

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References Cited [Referenced By]

U.S. Patent Documents

5854388	Dec., 1998	Harding et al.
6022696	Feb., 2000	Harding et al.
6066672	May, 2000	Kobori et al.

Other References

Carmicheal J, DeGraff WG, Gazdar AF, Minna JD, and Mitchell JB. Evaluation of tetrazolium-based, semi-automated colorimetric assay; assessment of radiosensitivity testing. *Cancer Res.* 47: 936-942, 1987.

Danielson, KG, LW Anderson, and HL Hosick. Selection and characterization in culture of mammary tumor cells with distinctive growth properties in vivo. *Cancer Res* 40: 1812-1819, 1980.

Hall, KL, S Venkateswaran, JM Hanesworth, ME Schelling, JW Harding. Characterization of a functional angiotensin IV receptor on coronary microvascular endothelial cells. *Regul Pept* 58: 107-15, 1995.

Kenemans P, Bosman A, Breast cancer and post-menopausal hormone therapy. *Best Pract Res Clin Endocrinol Metab.* 17:123-37, 2003.

Kerbel, R and Folkman, J. Clinical translation of angiogenesis inhibitors. *Nature reviews: Cancer* 2: 727-739, 2002.

Kramár, EA, DL Armstrong, S Ikeda, MJ Wayner, JW Harding, and JW Wright. 2001. The effects of angiotensin IV analogs on long-term potentiation within the CA1 region of the hippocampus *in vitro*. *Brain Res* 897: 114-121, 2001.

Morris EC, Bendle GM, Stauss HJ, Prospects for immunotherapy of malignant disease. *Clin Exp Immunol.* 131: 1-7, 2003.

O'Reilly MS, Holmgren L, Shing Y, Chen C, Rosenthal RA, Moses M, Lane WS, Cao Y, Sage EH, Folkman J. Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma.

Cell. 79:315-28, 1994.

Pastan I, Kreitman RJ. Immunotoxins in cancer therapy.

Curr Opin Investig Drugs. 3: 1089-91, 2002.

Sardinia, et al. AT₄ receptor binding relationship; N-terminal-modified angiotensin IV analogues. *Peptides* 15: 1399-1406, 1994.

Wright, JW, L Stubley, ES Pederson, EA Kramar, JM Hanesworth, JW Harding. Contributions of the brain angiotensin IV-AT₄ receptor subtype system to spatial learning. *J Neurosci* 19: 3952-61, 1999.

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Claims